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**********STN Columbus **********
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=> file medline embase biosis inpadoc caplus

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=> s skg/ab,bi

'AB' IS NOT A VALID FIELD CODE
L1      175 SKG/AB,BI

=> s l1 and (mouse or mice)(w)(strain#)/ab,bi

PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
'AB' IS NOT A VALID FIELD CODE
To see the field codes for search terms in an L-number, enter
"DISPLAY
QUERY" followed by the L-number at an arrow prompt. To see the
field
codes for search terms in a saved query, enter "ACTIVATE" and the
query name, followed by '/Q' at an arrow prompt.

=> s l1 and ((mouse or mice)(w)(strain#))/ab,bi

PROXIMITY OPERATION NOT ALLOWED
PROXIMITY OPERATION NOT ALLOWED
'AB' IS NOT A VALID FIELD CODE
To see the field codes for search terms in an L-number, enter
"DISPLAY
QUERY" followed by the L-number at an arrow prompt. To see the
field
codes for search terms in a saved query, enter "ACTIVATE" and the
query name, followed by '/Q' at an arrow prompt.

=> s l1 and mouse strain#/ab,bi

'AB' IS NOT A VALID FIELD CODE
L2       1 L1 AND MOUSE STRAIN#/AB,BI

=> d bib ab


L2  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2000 ACS
AN  1997:580424  CAPLUS
DN  127:246733
TI  A mouse model of rheumatoid arthritis
AU  Sakaguchi, Shimon
CS  Dep. Immunopathol., Tokyo Metrop. Inst. Gerontol., Tokyo, 173,
Japan
SO  Mol. Med. (Tokyo) (1997), 34(Suppl. 461), 214-221
    CODEN: MOLMEL; ISSN: 0918-6557
PB  Nakayama Shoten
DT  Journal; General Review
LA  Japanese
AB  A review with 20 refs. A ***mouse*** ***strain*** tentatively
    named ***SKG*** is a good model of human rheumatoid
arthritis, which
    originally derived from BALB/c mouse spontaneously exhibiting
arthrocele.
    The heredity is autosomal recessive. The mouse exhibits joint
anomaly
    with immunol. anomaly due to disorder in T cell prodn. in thymus.
    Adoptive transfer of spleen and lymph node cells to BALB/c nude
mouse
    generates the arthritis. Transplantation of T-cell depleted bone
marrow
    cells to nude mice generates arthritis by 2-4 mo irresp. to the
selection
    in host's thymus. Animal models of arthritis are described with
their
    characteristics ;antigen-sensitization, expression of a transgene in
    joints, T cell manipulation and MRL-/lpr/lpr. ***SKG***
mouse
    generates arthritis earlier and more evident than MRL-lpr/lpr, and
enables
    us to use BALB/c nude mouse.


=> e sakaguchi shimon/au

E1       1   SAKAGUCHI SHIHO/AU
E2       2   SAKAGUCHI SHIKAMORI/AU
E3      35 --> SAKAGUCHI SHIMON/AU
E4       1   SAKAGUCHI SHIMOONE/AU
E5       1   SAKAGUCHI SHIMOONE JIYUNKO/AU
E6       2   SAKAGUCHI SHIN/AU
E7       4   SAKAGUCHI SHIN ICHI/AU
E8       6   SAKAGUCHI SHINGO/AU
E9     115   SAKAGUCHI SHINICHI/AU
E10      1   SAKAGUCHI SHINICHI C O KABUSHI/AU
E11      3   SAKAGUCHI SHINICHIRO/AU
E12      3   SAKAGUCHI SHINICHIROU/AU

=> s e3

L3      35 "SAKAGUCHI SHIMON"/AU

=> s l3 and balb?/ab,bi

'AB' IS NOT A VALID FIELD CODE
L4       6 L3 AND BALB?/AB,BI

=> dup rem l4

PROCESSING COMPLETED FOR L4
L5       4 DUP REM L4 (2 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 4 ANSWERS -
CONTINUE? Y/(N):y


L5  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2000 ACS
AN  1997:580424  CAPLUS
DN  127:246733
TI  A mouse model of rheumatoid arthritis
AU  ***Sakaguchi, Shimon***
CS  Dep. Immunopathol., Tokyo Metrop. Inst. Gerontol., Tokyo, 173,
Japan
SO  Mol. Med. (Tokyo) (1997), 34(Suppl. 461), 214-221
    CODEN: MOLMEL; ISSN: 0918-6557
PB  Nakayama Shoten
DT  Journal; General Review
LA  Japanese
AB  A review with 20 refs. A mouse strain tentatively named SKG is
a good
    model of human rheumatoid arthritis, which originally derived from
    ***BALB*** /c mouse spontaneously exhibiting arthrocele.
The heredity is
    autosomal recessive. The mouse exhibits joint anomaly with
immunol.
    anomaly due to disorder in T cell prodn. in thymus. Adoptive
transfer of
    spleen and lymph node cells to ***BALB*** /c nude mouse
generates the
    arthritis. Transplantation of T-cell depleted bone marrow cells to
nude
    mice generates arthritis by 2-4 mo irresp. to the selection in host's
    thymus. Animal models of arthritis are described with their
    characteristics ;antigen-sensitization, expression of a transgene in
    joints, T cell manipulation and MRL-/lpr/lpr. SKG mouse
generates
    arthritis earlier and more evident than MRL-lpr/lpr, and enables us
to use
```

BALB /c nude mouse.

L5 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
AN 1995:409686 BIOSIS
DN PREV199598423986
TI Immunologic self-tolerance maintained by activated T cells expressing IL-2
receptor alpha-chains (CD25): Breakdown of a single mechanism of
self-tolerance causes various autoimmune diseases.
AU ***Sakaguchi, Shimon (1)*** ; Sakaguchi, Noriko; Asano, Masano; Itoh,
Misako; Toda, Masaaki
CS (1) Dep. Immunopathol., Tokyo Metropolitan Inst. Gerontol., 35-2 Sakaecho,
Itabashi-ku, Tokyo 173 Japan
SO Journal of Immunology, (1995) Vol. 155, No. 3, pp. 1151-1164.
ISSN: 0022-1767.
DT Article
LA English
AB Approximately 10% of peripheral CD4+ cells and less than 1% of CD8+ cells
in normal unimmunized adult mice express the IL-2 receptor alpha-chain
(CD25) molecules. When CD4+ cell suspensions prepared from ***BALB***
/c nu/+ mice lymph nodes and spleens were depleted of CD25+ cells by
specific mAb and C, and then inoculated into ***BALB*** /c athymic nude
(nu/nu) mice, all recipients spontaneously developed histologically and
serologically evident autoimmune diseases (such as thyroiditis, gastritis,
insulitis, sialoadenitis, adrenalitis, oophoritis, glomerulonephritis, and
polyarthritis); some mice also developed graft-vs-host-like wasting
disease. Reconstitution of CD4+CD25+ cells within a limited period after
transfer of CD4+CD25+ cells prevented these autoimmune developments in a
dose-dependent fashion, whereas the reconstitution several days later, or
inoculation of an equivalent dose of CD8+ cells, was far less efficient
for the prevention. When nu/nu mice were transplanted with allogeneic
skins or immunized with xenogeneic proteins at the time of CD25- cell
inoculation, they showed significantly heightened immune responses to the
skins or proteins, and reconstitution of CD4+CD25+ cells normalized the
responses. Taken together, these results indicate that CD4+CD25+ cells
contribute to maintaining self-tolerance by down-regulating immune
response to self and non-self Ags in an Ag-nonspecific manner, presumably
at the T cell activation stage; elimination/reduction of CD4+CD25+ cells
relieves this general suppression, thereby not only enhancing immune
responses to non-self Ags, but also eliciting autoimmune responses to
certain self-Ags. Abnormality of this T cell-mediated mechanism of
peripheral tolerance can be a possible cause of various autoimmune
diseases.

L5 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
AN 1994:110440 BIOSIS
DN PREV199497123440
TI Continuous administration of anti-interleukin 10 antibodies delays onset
of autoimmunity in NZB/W F-1 mice.
AU Ishida, Hiroshi; Muchamuel, Tony; ***Sakaguchi, Shimon*** ; Andrade,
Silvia; Menon, Satish; Howard, Maureen (1)
CS (1) DNAX Res. Inst., 901 California Ave., Palo Alto, CA 94304 USA
SO Journal of Experimental Medicine, (1994) Vol. 179, No. 1, pp. 305-310.
ISSN: 0022-1007.
DT Article
LA English
AB We have previously shown that continuous administration of
anti-interleukin 10 (anti-IL-10) antibodies (Abs) to ***BALB*** /c mice
modifies endogenous levels of autoantibodies, tumor necrosis factor alpha
(TNF-alpha), and interferon gamma, three immune mediators known to affect
the development of autoimmunity in "lupus-prone" New Zealand black/white
(NZB/W)F-1 mice. To explore the consequences of IL-10 neutralization in
NZB/W F-1 mice, animals were injected two to three times per week from
birth until 8-10 mo of age with anti-IL-10 Abs or with isotype control
Abs. Anti-IL-10 treatment substantially delayed onset of autoimmunity in
NZB/W F-1 mice as monitored either by overall survival, or by development
of proteinuria, glomerulonephritis, or autoantibodies. Survival at 9 mo
was increased from 10 to 80% in anti-IL-10-treated mice relative to Ig
isotype-treated controls. This protection against autoimmunity appeared to
be due to an anti-IL-10-induced upregulation of endogenous TNF-alpha,
since anti-IL-10-protected NZB/W F-1 mice rapidly developed autoimmunity
when neutralizing anti-TNF-alpha Abs were introduced at 30 wk along with
the anti-IL-10 treatment. Consistent with the protective role of
anti-IL-10 treatment in these experiments, continuous administration of
IL-10 from 4 until 38 wk of age accelerated the onset of autoimmunity in
NZB/W F-1 mice. The same period of continuous IL-10 administration did not
appear to be toxic to, or cause development of lupus-like autoimmunity in
normal ***BALB*** /c mice. These data suggest that IL-10 antagonists
may be beneficial in the treatment of human systemic lupus erythematosus.

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2000 ACS
AN 1989:88194 CAPLUS
DN 110:88194
TI Organ-specific autoimmune disease induced in mice by elimination of T cell
subsets. V. Neonatal administration of cyclosporin A causes autoimmune
disease
AU ***Sakaguchi, Shimon*** ; Sakaguchi, Noriko
CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO J. Immunol. (1989), 142(2), 471-80
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
AB Cyclosporin A (CsA), a potent immunosuppressive drug, caused
organ-specific autoimmune disease, such as gastritis with anti-parietal
cell autoantibodies or oophoritis with anti-ooctye autoantibodies, in
BALB /c mice when the drug was administered daily for 1 wk to
newborns. Administration to adult mice did not have this effect. CsA
abrogated the prodn. of L3T4+ T cells and Lyt-2+T cells in the thymus.
These T cells were substantially deleted from the peripheral lymphoid
organs, esp. when the drug was administered from the day of birth.
Autoimmune disease was prevented when CsA-treated newborn mice were
inoculated with splenic T cells from normal syngeneic mice. Removal of
the thymus immediately after neonatal CsA treatment produced autoimmune
disease with a higher incidence and in a wider spectrum of organs, i.e.,
thyroiditis, sialoadenitis, gastritis, insulitis, epinephritis,
oophoritis, or orchitis. Each autoimmune disease was accompanied by the
development of circulating autoantibodies specific for the

corresponding
organ antigens. Immunopathol. of these autoimmune diseases was similar to
that of human organ-specific autoimmune diseases.

=> d his

(FILE 'HOME' ENTERED AT 14:54:45 ON 24 JUL 2000)

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 14:56:07 ON 24
JUL 2000
L1 175 S SKG/AB,BI
L2 1 S L1 AND MOUSE STRAIN#/AB,BI
E SAKAGUCHI SHIMON/AU
L3 35 S E3
L4 6 S L3 AND BALB?/AB,BI
L5 4 DUP REM L4 (2 DUPLICATES REMOVED)

=> e sakaguchi s/au

E1 1 SAKAGUCHI RYUII/AU
E2 18 SAKAGUCHI RYUJI/AU
E3 823 --> SAKAGUCHI S/AU
E4 4 SAKAGUCHI S I/AU
E5 1 SAKAGUCHI SACHIHIRO/AU
E6 6 SAKAGUCHI SACHIKO/AU
E7 1 SAKAGUCHI SADAHIKO/AU
E8 4 SAKAGUCHI SADANORI/AU
E9 2 SAKAGUCHI SADAO/AU
E10 1 SAKAGUCHI SAI/AU
E11 1 SAKAGUCHI SAKAGUCHI/AU
E12 4 SAKAGUCHI SAKUYA/AU

=> s e3

L6 823 "SAKAGUCHI S"/AU

=> s l6 and balb?/ab,bi

'AB' IS NOT A VALID FIELD CODE
L7 36 L6 AND BALB?/AB,BI

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8 23 DUP REM L7 (13 DUPLICATES REMOVED)

=> d 1- biba b

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'B' IS NOT A VALID FORMAT
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YOU HAVE REQUESTED DATA FROM 23 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 23 MEDLINE
AN 1999244897 MEDLINE
DN 99244897
TI Thymus and autoimmunity: production of CD25+CD4+ naturally anergic and
suppressive T cells as a key function of the thymus in maintaining immunologic self-tolerance.
AU Itoh M; Takahashi T; Sakaguchi N; Kuniyasu Y; Shimizu J; Otsuka F;
Sakaguchi S
CS Department of Immunopathology, Tokyo Metropolitan Institute of
Gerontology, Japan.
SO JOURNAL OF IMMUNOLOGY, (1999 May 1) 162 (9) 5317-26.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199907
EW 19990704
AB This study shows that the normal thymus produces immunoregulatory
CD25+4+8- thymocytes capable of controlling self-reactive T cells. Transfer of thymocyte suspensions depleted of CD25+4+8- thymocytes, which
constitute approximately 5% of steroid-resistant mature CD4+8- thymocytes
in normal naive mice, produces various autoimmune diseases in syngeneic
athymic nude mice. These CD25+4+8- thymocytes are nonproliferative
(anergic) to TCR stimulation in vitro, but potently suppress the proliferation of other CD4+8- or CD4-8+ thymocytes; breakage of their
anergic state in vitro by high doses of IL-2 or anti-CD28 Ab
simultaneously abrogates their suppressive activity; and transfer of such
suppression-abrogated thymocyte suspensions produces autoimmune disease in
nude mice. These immunoregulatory CD25+4+8- thymocytes/T cells are
functionally distinct from activated CD25+4+ T cells derived from CD25-4+
thymocytes/T cells in that the latter scarcely exhibits suppressive activity in vitro, although both CD25+4+ populations express a similar
profile of cell surface markers. Furthermore, the CD25+4+8- thymocytes
appear to acquire their anergic and suppressive property through the thymic selection process, since TCR transgenic mice develop similar
anergic/suppressive CD25+4+8- thymocytes and CD25+4+ T cells that
predominantly express TCRs utilizing endogenous alpha-chains, but
RAG-2-deficient TCR transgenic mice do not. These results taken together
indicate that anergic/suppressive CD25+4+8- thymocytes and peripheral T
cells in normal naive mice may constitute a common T cell lineage
functionally and developmentally distinct from other T cells, and that
production of this unique immunoregulatory T cell population can be
another key function of the thymus in maintaining immunologic self-tolerance.

L8 ANSWER 2 OF 23 MEDLINE
AN 1999244896 MEDLINE
DN 99244896
TI Virus and autoimmunity: induction of autoimmune disease in mice by mouse T
lymphotropic virus (MTLV) destroying CD4+ T cells.
AU Morse S S; Sakaguchi N; ***Sakaguchi S***
CS The Rockefeller University, New York 10021, USA.
SO JOURNAL OF IMMUNOLOGY, (1999 May 1) 162 (9) 5309-16.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199907
EW 19990704
AB Neonatal infection of the mouse T lymphotropic virus (MTLV), a member of
herpes viridae, causes various organ-specific autoimmune diseases, such as
autoimmune gastritis, in selected strains of normal mice. The infection
selectively depletes CD4+ T cells in the thymus and periphery for 2-3 wk
from 1 wk after infection. Thymectomy 3 wk after neonatal MTLV infection
enhances the autoimmune responses and produces autoimmune diseases at
higher incidences and in a wider spectrum of organs than MTLV infection
alone. On the other hand, inoculation of peripheral CD4+ cells from syngeneic noninfected adult mice prevents the autoimmune development.
These autoimmune diseases can be adoptively transferred to

syngeneic
athymic nude mice by CD4+ T cells. The virus is not detected by bioassay
in the organs/tissues damaged by the autoimmune responses. Furthermore,
similar autoimmune diseases can be induced in normal mice by manipulating
the neonatal thymus/T cells (e.g., by neonatal thymectomy) without virus
infection. These results taken together indicate that neonatal MTLV
infection elicits autoimmune disease by primarily affecting thymocytes/T
cells, not self Ags. It may provoke or enhance thymic production of CD4+
pathogenic self-reactive T cells by altering the thymic clonal deletion
mechanism, or reduce the production of CD4+ regulatory T cells controlling
self-reactive T cells, or both. The possibility is discussed that other T
cell-tropic viruses may cause autoimmunity in humans and animals by
affecting the T cell immune system, not the self Ags to be targeted by the
autoimmunity.

L8 ANSWER 3 OF 23 MEDLINE
AN 2000021812 MEDLINE
DN 20021812
TI Induction of tumor immunity by removing CD25+CD4+ T cells: a common basis
between tumor immunity and autoimmunity.
AU Shimizu J; Yamazaki S; ***Sakaguchi S***
CS Department of Immunopathology, Tokyo Metropolitan Institute of
Gerontology, Japan.
SO JOURNAL OF IMMUNOLOGY, (1999 Nov 15) 163 (10) 5211-8.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 200002
EW 20000204
AB This study shows that removal of a T cell subpopulation can evoke
effective tumor immunity in otherwise nonresponding animals. Elimination
of CD25-expressing T cells, which constitute 5-10% of peripheral CD4+ T
cells in normal naive mice, elicited potent immune responses to syngeneic
tumors in vivo and eradicated them. The responses were mediated by
tumor-specific CD8+ CTLs and tumor-nonspecific CD4-8- cytotoxic cells akin
to NK cells. Furthermore, in vitro culture of CD25+4+ T cell-depleted
splenic cell suspensions prepared from tumor-unsensitized normal mice led
to spontaneous generation of similar CD4-8- cytotoxic cells capable of
killing a broad spectrum of tumors; reconstitution of CD25+4+ T cells
inhibited the generation. In this culture, self-reactive CD25-4+ T cells
responding to self peptides/class II MHC complexes on APCs spontaneously
proliferated upon removal of CD25+4+ T cells, secreting large amounts of
IL-2. The IL-2 thus produced appeared to be responsible for the generation
of CD4-8- NK cells as lymphokine-activated killer cells, because direct
addition of an equivalent amount of IL-2 to the culture of CD4-8- cells
generated similar lymphokine-activated killer/NK cells, whereas coculture
of normal CD4-8- cells with CD25-4+ T cells from IL-2-deficient mice did
not. Thus, removal of immunoregulatory CD25+4+ T cells can abrogate
immunological unresponsiveness to syngeneic tumors in vivo and in vitro,
leading to spontaneous development of tumor-specific effector cells as
well as tumor-nonspecific ones. This novel way of evoking tumor immunity
would help to devise effective immunotherapy for cancer in humans.

L8 ANSWER 4 OF 23 MEDLINE
AN 1999323384 MEDLINE
DN 99323384
TI Tumor rejection by in vivo administration of anti-CD25 (interleukin-2
receptor alpha) monoclonal antibody.
AU Onizuka S; Tawara I; Shimizu J; ***Sakaguchi S*** ; Fujita T; Nakayama
E
CS Department of Parasitology and Immunology, Okayama University Medical
School, Japan.
SO CANCER RESEARCH, (1999 Jul 1) 59 (13) 3128-33.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199909
EW 19990905
AB Immune regulation has been shown to be involved in the progressive growth
of some murine tumors. In this study, we demonstrated that a single in
vivo administration of an amount less than 0.125 mg of anti-CD25
interleukin 2 receptor alpha monoclonal antibody (mAb; PC61) caused the
regression of tumors that grew progressively in syngeneic mice. The tumors
used were five leukemias, a myeloma, and two sarcomas derived from four
different inbred mouse strains. Anti-CD25 mAb (PC61) showed an effect in
six of the eight tumors. Administration of anti-CD25 mAb (PC61) caused a
reduction in the number of CD4+ CD25+ cells in the peripheral lymphoid
tissues. The findings suggested that CD4+ CD25+ immunoregulatory cells
were involved in the growth of those tumors. Kinetic analysis showed that
the administration of anti-CD25 mAb (PC61) later than day 2 after tumor
inoculation caused no tumor regression, irrespective of depletion of CD4+
CD25+ immunoregulatory cells. Two leukemias, on which the PC61-treatment
had no effect, seemed to be incapable of eliciting effective rejection
responses in the recipient mice because of low or no antigenicity.

L8 ANSWER 5 OF 23 MEDLINE
AN 1999101009 MEDLINE
DN 99101009
TI Immunologic self-tolerance maintained by CD25+CD4+ naturally anergic and
suppressive T cells: induction of autoimmune disease by breaking their
anergic/suppressive state.
AU Takahashi T; Kuniyasu Y; Toda M; Sakaguchi N; Itoh M; Iwata M; Shimizu J;
Sakaguchi S
CS Department of Immunopathology, Tokyo Metropolitan Institute of
Gerontology, Japan.
SO INTERNATIONAL IMMUNOLOGY, (1998 Dec) 10 (12) 1969-80.
Journal code: AY5. ISSN: 0953-8178.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
EW 19990504
AB Elimination of CD25+ T cells, which constitute 5-10% of peripheral CD4+ T
cells in normal naive mice, leads to spontaneous development of various

autoimmune diseases. These immunoregulatory CD25+CD4+ T cells are naturally unresponsive (anergic) in vitro to TCR stimulation, and, upon stimulation, suppress proliferation of CD25-CD4+ T cells and CD8+ T cells. The antigen concentration required for stimulating CD25+CD4+ T cells to exert suppression is much lower than that required for stimulating CD25-CD4+ T cells to proliferate. The suppression, which results in reduced IL-2 production by CD25-CD4+ T cells, is dependent on cellular interactions on antigen-presenting cells (and not mediated by far-reaching or long-lasting humoral factors or apoptosis-inducing signals) and antigen non-specific in its effector phase. Addition of high doses of IL-2 or anti-CD28 antibody to the in vitro T cell stimulation culture not only breaks the anergic state of CD25+CD4+ T cells, but also abrogates their suppressive activity simultaneously. Importantly, the anergic/suppressive state of CD25+CD4+ T cells appeared to be their basal default condition, since removal of IL-2 or anti-CD28 antibody from the culture milieu allows them to revert to the original anergic/suppressive state. Furthermore, transfer of such anergy/suppression-broken T cells from normal mice produces various autoimmune diseases in syngeneic athymic nude mice. These results taken together indicate that one aspect of immunologic self-tolerance is maintained by this unique CD25+CD4+ naturally anergic/suppressive T cell population and its functional abnormality directly leads to the development of autoimmune disease.

L8 ANSWER 6 OF 23 MEDLINE
AN 97108846 MEDLINE
DN 97108846
TI Effects of antitumor activity and protection of shock symptoms by a traditional Chinese medicine (sho-saiko-to) in recombinant human tumor necrosis factor administered mice.
AU ***Sakaguchi S*** ; Furusawa S; Yokota K; Sasaki K; Takayanagi M; Takayanagi Y
CS First Department of Hygienic Chemistry, Tohoku College of Pharmacy, Sendai, Japan.
SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (1996 Nov) 19 (11) 1474-8.
Journal code: BPZ. ISSN: 0918-6158.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970504
AB The effects of a traditional Chinese medicine Sho-saiko-to (Kampo prescription) were investigated on the various metabolic disorders and antitumor activity of recombinant human tumor necrosis factor (rhTNF) administered to mice. The glycogen level in liver of rhTNF (5 x 10(4) units/mouse, i.v.)-injected mice was markedly lower at 4 h post-intoxication than that in the control, whereas the administration of rhTNF to Sho-saiko-to (500 mg/kg/d, p.o.)-pretreated mice resulted in a greater level of glycogen than that in rhTNF alone-treated mice. In mice pretreated with Sho-saiko-to, the level of fibrinogen 4 h after rhTNF injection markedly increased as compared to that in mice treated with rhTNF alone. We also estimated the NO2 in murine macrophage cell line J774A.1 using mice serum after administration of Sho-saiko-to. Our results clearly demonstrated that J774A.1 cells stimulated with endotoxin (1 micrograms/ml) and rhTNF (1 x 10(4) units/ml) can effectively produce nitric oxide (NO), and ascertained the suppressive effect of Sho-saiko-to (500 mg/kg/d, p.o)-pretreated serum on NO generation by endotoxin/TNF-activated J774A.1 cells. When the cells were incubated with endotoxin/TNF and Sho-saiko-to pretreated serum (10-100 microliters), the NO level was significantly lower than that in control serum incubated with endotoxin/TNF alone. The effect of Sho-saiko-to (1 and 10 micrograms/ml) on in vitro cytotoxicity by rhTNF in Meth-A Sarcoma cells was observed to be in a dose dependent fashion. In addition, there was a remarkable enhancement of antitumor activity of rhTNF by Sho-saiko-to pretreatment in mice. These findings suggest that the Kampo prescription Sho-saiko-to may protect mice from severe shock syndrome by rhTNF, and that it may enhance rhTNF-induced activity.

L8 ANSWER 7 OF 23 MEDLINE
AN 96307805 MEDLINE
DN 96307805
TI The changes of complement activities in sera of mice after subcutaneous administration of beryllium chloride.
AU Sakaguchi T; ***Sakaguchi S*** ; Nakamura I; Kudo Y
CS Department of Hygiene, St. Marianna University School of Medicine, Kawasaki, Japan.
SO NIPPON EISEIGAKU ZASSHI. JAPANESE JOURNAL OF HYGIENE, (1996 Feb) 50 (6) 1077-83.
Journal code: KKN. ISSN: 0021-5082.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199612
AB We studied changes of the complement pathway activities and the content of C3 in sera of mice, administered BeCl2 (containing 5 micrograms of Be per mouse) or CuCl2 (containing 5 micrograms of Cu per mouse) by a single subcutaneous injection. The value of the classical complement pathway activity (CH50) of the Be group 3 days after administration was significantly higher than that of the control group ($P < 0.001$). It was significantly lower than in the control group after 7 days ($P < 0.001$). On the other hand, the CH50 value of the Cu group 3 hr after administration tended to increase, however, it was significantly lower than in the control group after 7 days ($P < 0.01$). The change of the alternative complement pathway activity (ACH50) value of the Be group was similar to the change of the CH50 value of the group. The ACH50 value of the Cu group 3 days after administration tended to increase but it was the same as the ACH50 value of the control group after 7 days. The C3 contents of both the Be and Cu groups 3 days after administration were significantly higher than in the control group ($P < 0.001$). The aspartate aminotransferase (AST) activity of the Be group 7 days after administration was significantly higher than that of the control group ($P < 0.01$). By contrast, AST activity of the Cu group 3 hr after administration was significantly higher than in the control group ($P < 0.05$). The value of the alanine aminotransferase (ALT) activity of the Be group was low ($P < 0.01$), but that of the Cu group was high ($P < 0.05$), 3 hr after administration. These values of both groups after 7 days, however, were significantly higher than in the control group ($P < 0.05$). The AST/ALT ratio in mice was very high at 3 hr, and it remained high by 7 days

after
Be injection. On the other hand, the ratio of the Cu group was almost
constant for 7 days after Cu injection. Thus, these values changed with
relative expedition after Be injection. Therefore, we confirmed that
measurements of complement activities and the content of C3 were valuable
indices for assaying acute effects of Be on mice.

L8 ANSWER 8 OF 23 MEDLINE
AN 96343849 MEDLINE
DN 96343849
TI Autoimmune disease as a consequence of developmental abnormality of a T
cell subpopulation.
AU Asano M; Toda M; Sakaguchi N; ***Sakaguchi S***
CS Department of Immunopathology, Tokyo Metropolitan Institute of Geromology,
Japan.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Aug 1) 184 (2) 387-96.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199611
AB Neonatal thymectomy (NTx), especially around day 3 after birth, causes
various organ-specific autoimmune diseases in mice. This report shows
that: (a) T cells expressing the interleukin 2 receptor alpha chains
(CD25) ontogenically begin to appear in the normal periphery immediately
after day 3, rapidly increasing within 2 wk to nearly adult levels
(approximately 10% of CD3+ cells, especially of CD4+ cells); (b) NTx on
day 3 eliminates CD25+ T cells from the periphery for several days;
inoculation immediately after NTx of CD25+ splenic T cells from syngeneic
non-Tx adult mice prevents autoimmune development, whereas inoculation of
CD25- T cells even at a larger dose does not; and furthermore, (c) similar
autoimmune diseases can be produced in adult athymic nu/nu mice by
inoculating either spleen cell suspensions from 3-d-old euthymic nu/+ mice
or CD25+ cell-depleted spleen cell suspensions from older, even 1-yr-old,
nu/+ mice. The CD25- populations from neonates or adults are also similar
in the profile of cytokine formation. These results, taken together,
indicate that one aspect of peripheral self-tolerance is maintained by
CD25+ T cells that sustain potentially pathogenic self-reactive T cells in
a CD25- dormant state; the thymic production of the former is
developmentally programmed to begin on day 3 after birth in mice. Thus,
NTx on day 3 can, at least transiently, eliminate/reduce the
autoimmune-preventive CD25+ T cells, thereby leading to activation of the
self-reactive T cells that have been produced before NTx.

L8 ANSWER 9 OF 23 MEDLINE DUPLICATE 1
AN 95363080 MEDLINE
DN 95363080
TI Immunologic self-tolerance maintained by activated T cells expressing IL-2
receptor alpha-chains (CD25). Breakdown of a single mechanism of
self-tolerance causes various autoimmune diseases.
AU ***Sakaguchi S*** ; Sakaguchi N; Asano M; Itoh M; Toda M
CS Precursory Research for Embryonic Science and Technology (PRESTO),
Research and Development Corporation of Japan (JRDC), Tsukuba Life Science
Center.
SO JOURNAL OF IMMUNOLOGY, (1995 Aug 1) 155 (3) 1151-64.

Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199511
AB Approximately 10% of peripheral CD4+ cells and less than 1% of CD8+ cells
in normal unimmunized adult mice express the IL-2 receptor alpha-chain
(CD25) molecules. When CD4+ cell suspensions prepared from ***BALB***
/c nu/+ mice lymph nodes and spleens were depleted of CD25+ cells by
specific mAb and C, and then inoculated into ***BALB*** /c athymic nude
(nu/nu) mice, all recipients spontaneously developed histologically and
serologically evident autoimmune diseases (such as thyroiditis, gastritis,
insulitis, sialoadenitis, adrenalitis, oophoritis, glomerulonephritis, and
polyarthritis); some mice also developed graft-vs-host-like wasting
disease. Reconstitution of CD4+CD25+ cells within a limited period after
transfer of CD4+CD25- cells prevented these autoimmune developments in a
dose-dependent fashion, whereas the reconstitution several days later, or
inoculation of an equivalent dose of CD8+ cells, was far less efficient
for the prevention. When nu/nu mice were transplanted with allogeneic
skins or immunized with xenogeneic proteins at the time of CD25- cell
inoculation, they showed significantly heightened immune responses to the
skins or proteins, and reconstitution of CD4+CD25+ cells normalized the
responses. Taken together, these results indicate that CD4+CD25+ cells
contribute to maintaining self-tolerance by down-regulating immune
response to self and non-self Ags in an Ag-nonspecific manner, presumably
at the T cell activation stage; elimination/reduction of CD4+CD25+ cells
relieves this general suppression, thereby not only enhancing immune
responses to non-self Ags, but also eliciting autoimmune responses to
certain self-Ags. Abnormality of this T cell-mediated mechanism of
peripheral tolerance can be a possible cause of various autoimmune
diseases.

L8 ANSWER 10 OF 23 MEDLINE
AN 94179843 MEDLINE
DN 94179843
TI Ionizing radiation and autoimmunity. Induction of autoimmune disease in
mice by high dose fractionated total lymphoid irradiation and its
prevention by inoculating normal T cells.
AU Sakaguchi N; Miyai K; ***Sakaguchi S***
CS Department of Medicine, Stanford University School of Medicine, CA 94305.
SO JOURNAL OF IMMUNOLOGY, (1994 Mar 1) 152 (5) 2586-95.

Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199406
AB Ionizing radiation can functionally alter the immune system and break
self-tolerance. High dose (42.5 Gy), fractionated (2.5 Gy 17 times) total
lymphoid irradiation (TLI) on mice caused various organ-specific
autoimmune diseases, such as gastritis, thyroiditis, and orchitis,
depending on the radiation dosages, the extent of lymphoid irradiation,
and the genetic background of the mouse strains. Radiation-induced tissue
damage is not the primary cause of the autoimmune disease because
irradiation of the target organs alone failed to elicit the autoimmunity
and shielding of the organs from irradiation was unable to prevent

it. In
contrast, irradiation of both the thymus and the peripheral lymphoid
organs/tissues was required for efficient induction of autoimmune disease
by TLI. TLI eliminated the majority of mature thymocytes and the
peripheral T cells for 1 mo, and inoculation of spleen cell, thymocyte, or
bone marrow cell suspensions (prepared from syngeneic nonirradiated mice)
within 2 wk after TLI effectively prevented the autoimmune development.
Depletion of T cells from the inocula abrogated the preventive activity.
CD4+ T cells mediated the autoimmune prevention but CD8+ T cells did not.
CD4+ T cells also appeared to mediate the TLI-induced autoimmune disease
because CD4+ T cells from disease-bearing TLI mice adoptively transferred
the autoimmune disease to syngeneic naive mice. Taken together, these
results indicate that high dose, fractionated ionizing radiation on the
lymphoid organs/tissues can cause autoimmune disease by affecting the T
cell immune system, rather than the target self-Ags, presumably by
altering T cell-dependent control of self-reactive T cells.

L8 ANSWER 11 OF 23 MEDLINE DUPLICATE 2
AN 94095937 MEDLINE
DN 94095937
TI Continuous administration of anti-interleukin 10 antibodies delays onset
of autoimmunity in NZB/W F1 mice.
AU Ishida H; Muchamuel T; ***Sakaguchi S*** ; Andrade S; Menon S; Howard M
CS DNAX Research Institute, Palo Alto, California 94304..
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1994 Jan 1) 179 (1) 305-10.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199404
AB We have previously shown that continuous administration of
anti-interleukin 10 (anti-IL-10) antibodies (Abs) to ***BALB*** /c mice
modifies endogenous levels of autoantibodies, tumor necrosis factor alpha
(TNF-alpha), and interferon gamma, three immune mediators known to affect
the development of autoimmunity in "lupus-prone" New Zealand black/white
(NZB/W)F1 mice. To explore the consequences of IL-10 neutralization in
NZB/W F1 mice, animals were injected two to three times per week from
birth until 8-10 mo of age with anti-IL-10 Abs or with isotype control
Abs. Anti-IL-10 treatment substantially delayed onset of autoimmunity in
NZB/W F1 mice as monitored either by overall survival, or by development
of proteinuria, glomerulonephritis, or autoantibodies. Survival at 9 mo
was increased from 10 to 80% in anti-IL-10-treated mice relative to Ig
isotype-treated controls. This protection against autoimmunity appeared to
be due to an anti-IL-10-induced upregulation of endogenous TNF-alpha,
since anti-IL-10-protected NZB/W F1 mice rapidly developed autoimmunity
when neutralizing anti-TNF-alpha Abs were introduced at 30 wk along with
the anti-IL-10 treatment. Consistent with the protective role of
anti-IL-10 treatment in these experiments, continuous administration of
IL-10 from 4 until 38 wk of age accelerated the onset of autoimmunity in
NZB/W F1 mice. The same period of continuous IL-10 administration did not
appear to be toxic to, or cause development of lupus-like autoimmunity in
normal ***BALB*** /c mice. These data suggest that IL-10 antagonists
may be beneficial in the treatment of human systemic lupus erythematosus.

L8 ANSWER 12 OF 23 MEDLINE DUPLICATE 3
AN 90324874 MEDLINE
DN 90324874
TI Thymus and autoimmunity: capacity of the normal thymus to produce
pathogenic self-reactive T cells and conditions required for their
induction of autoimmune disease.
AU ***Sakaguchi S*** ; Sakaguchi N
CS Department of Immunology, Research Institute of Scripps Clinic, La Jolla,
California 92037..
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1990 Aug 1) 172 (2) 537-45.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199011
AB ***BALB*** /c athymic nu/nu mice spontaneously developed organ-specific
(gastritis, thyroiditis, oophoritis, or orchitis) and systemic (arteritis,
glomerulonephritis, and polyarthritis) autoimmune diseases when
transplanted with neonatal ***BALB*** /c thymuses. Transplantation of
thymuses from adult ***BALB*** /c mice was far less effective in
inducing histologically evident organ-specific autoimmune disease in nu/nu
mice. Autoimmune disease developed, however, when adult thymuses were
irradiated at a T cell-depleting dose before transplantation. Engrafting
newborn thymuses into ***BALB*** /c mice T cell depleted by thymectomy,
irradiation, and bone marrow transplantation produced similar
organ-specific autoimmune disease as well, but thymus engrafting into T
cell-nondepleted ***BALB*** /c mice (i.e., mice thymectomized as
adults, but not irradiated) did not, despite the fact that transplanted
thymuses grew well in both groups of mice. The mice with organ-specific
autoimmune disease produced autoantibodies specific for the respective
organ components, such as gastric parietal cells, thyroglobulins, oocytes,
or sperm. The thymus-transplanted nu/nu mice also had
hypergammaglobulinemia and developed anti-DNA autoantibodies, rheumatoid
factors, and immune complexes in the circulation. These results indicate
that: (a) the thymus of a murine strain that does not develop spontaneous
autoimmune disease can produce pathogenic self-reactive T cells that
mediate organ-specific and/or systemic autoimmune diseases; and (b) such
self-reactive T cells, especially those mediating organ-specific
autoimmune disease, spontaneously expand and cause autoimmune disease when
released to the T cell-deficient or -eliminated periphery.

L8 ANSWER 13 OF 23 MEDLINE
AN 89286150 MEDLINE
DN 89286150
TI Importance of the conjugated antibody for the induction of selective
effect of adriamycin conjugated with anti AFP monoclonal antibody and
entrapped in liposomes against AFP producing tumors.
AU Konno H; Kumai K; Tsubouchi T; Ishibiki K; Abe O; Tadakuma T; Yasuda T;
Nagaike K; Hosokawa S; ***Sakaguchi S***
CS 2nd Dept. of Surgery, Hamamatsu University..
SO GAN TO KAGAKU RYOHO [JAPANESE JOURNAL OF CANCER AND CHEMOTHERAPY], (1989
Jun) 16 (6) 2213-7.
Journal code: 6T8. ISSN: 0385-0684.
CY Japan

DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals; Cancer Journals
EM 198909
AB We investigated experimentally the effect of adriamycin (ADM) conjugated
with anti alpha-fetoprotein (AFP) monoclonal antibodies and entrapped in
liposomes (Lip-ADM = AbAFP) in vitro or in vivo. In the present study, we
examined the importance of the conjugated antibody for the induction of
selective therapeutic effect of Lip-ADM = AbAFP against AFP producing
tumors. As the target tumors, AFP producing human hepatoma strain, Li-7,
and AFP non-producing human breast cancer strain, MX-1 maintained in
BALB /c nu/nu male mice were used. In order to evaluate the
importance of the conjugated antibody, we prepared also ADM conjugated
with normal mouse IgG, and entrapped in liposomes Lip-ADM = NIgG, of which
therapeutic effects were compared with that of Lip-ADM = AbAFP. Judging
from the tumor growth curve and the tumor weight, the therapeutic effect
of Lip-ADM = AbAFP was greater against Li-7 than that of Lip-ADM = NIgG.
On the other hand, both conjugates showed similar effects against MX-1. As
the results it is suggested that the antibody which recognizes the antigen
expressed on the target tumor cells can solely increase the therapeutic
effect of ADM entrapped in liposomes (Lip-ADM) and that the main factors
which contribute to the efficient therapeutic effect of the conjugate were
the sensitibility to ADM, the affinity of the tumor cells to liposomes and
the superiority of the conjugated antibody.

L8 ANSWER 14 OF 23 MEDLINE DUPLICATE 4
AN 89093928 MEDLINE
DN 89093928
TI Organ-specific autoimmune disease induced in mice by elimination of T cell
subsets. V. Neonatal administration of cyclosporin A causes autoimmune
disease.
AU ***Sakaguchi S*** ; Sakaguchi N
CS Department of Biophysics, Johns Hopkins University School of Medicine,
Baltimore, MD 21205..
SO JOURNAL OF IMMUNOLOGY, (1989 Jan 15) 142 (2) 471-80.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198904
AB Cyclosporin A (CsA), a potent immunosuppressive drug, caused
organ-specific autoimmune disease, such as gastritis with anti-parietal
cell autoantibodies or oophoritis with anti-oocyte autoantibodies, in
BALB /c mice when the drug was administered daily for 1 wk to
newborns. Administration to adult mice did not. CsA abrogated the
production of L3T4+ T cells and Lyt-2+ T cells in the thymus.
Consequently, these T cells were substantially depleted from the
peripheral lymphoid organs, especially when the drug was administered from
the day of birth. Autoimmune disease was prevented when CsA-treated
newborn mice were inoculated with splenic T cells from normal syngeneic
mice. However, removal of the thymus immediately after neonatal CsA
treatment produced autoimmune disease with a higher incidence and in a
wider spectrum of organs, i.e., thyroiditis, sialoadenitis of the salivary
gland, gastritis, insulitis of the endocrine pancreas, adrenalitis,
oophoritis, or orchitis. Each autoimmune disease was accompanied by the
development of circulating autoantibodies specific for the corresponding
organ Ag. Immunopathology of these autoimmune diseases was quite similar
to that of human organ-specific autoimmune diseases.

L8 ANSWER 15 OF 23 MEDLINE
AN 88187613 MEDLINE
DN 88187613
TI Thymus and autoimmunity. Transplantation of the thymus from cyclosporin
A-treated mice causes organ-specific autoimmune disease in athymic nude
mice.
AU ***Sakaguchi S*** ; Sakaguchi N
CS Department of Biophysics, Johns Hopkins University School of Medicine,
Baltimore, Maryland 21205..
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Apr 1) 167 (4) 1479-85.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198807
AB Organ-specific autoimmune diseases such as gastritis, oophoritis,
thyroiditis, or insulitis developed in athymic nu/nu mice after
engraftment of the thymus from euthymic nu/+ mice treated with cyclosporin
A (CsA), a potent immuno-suppressant. The development of autoimmune
disease in the nu/nu mice was prevented by inoculation of thymocyte
suspensions prepared from normal nu/+ mice, but not by thymocyte
suspensions from CsA-treated nu/+ mice. Cotransplantation of normal nu/+
mouse thymus with CsA-treated thymus also suppressed the development of
autoimmune disease. Inoculation of spleen cell suspensions prepared from
normal adult nu/+ mice prevented autoimmune disease, but inoculation of
those from newborn nu/+ mice did not. Thus, CsA appears to interfere
selectively with the thymic production of certain suppressor T cells
controlling self-reactive (autoimmune) T cells, allowing the latter to
expand and cause autoimmune disease.

L8 ANSWER 16 OF 23 MEDLINE DUPLICATE 5
AN 88084259 MEDLINE
DN 88084259
TI Immunologic and clinical studies on murine experimental autoimmune
gastritis induced by neonatal thymectomy.
AU Fukuma K; ***Sakaguchi S*** ; Kuribayashi K; Chen W L; Morishita R;
Sekita K; Uchino H; Masuda T
CS Department of Immunobiology, Faculty of Medicine, Kyoto University,
Japan..
SO GASTROENTEROLOGY, (1988 Feb) 94 (2) 274-83.
Journal code: FH3. ISSN: 0016-5085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198804
AB Experimental autoimmune gastritis (AIG), defined by the appearance of auto
antibodies to parietal cells, was induced by neonatal thymectomy in
BALB /c nu/+mice 3 days after birth. Vitamin B12 absorption and
intrinsic factor in the stomach extract decreased compared with those in
AIG-negative control groups. No decrease of the serum A/G ratio in
AIG-bearing mice was observed. Although development of anemia, as
evaluated by a decrease in hematocrit value, was poor until 12 mo

of age
and the gastric mucosa was hypertrophic, the AIG resembled human
pernicious anemia rather than Menetrier's disease. Adoptive transfer of
spleen cells, but not sera, of AIG-bearing nu/+ into ***BALB*** /c
nu/nu mice caused AIG in all animals 1 mo later, indicating the involvement of lymphocytes in the induction mechanism of AIG.
Cytofluorometric and immunohistochemical analysis of lymphocytes in the
gastric mucosa revealed T-cell infiltration at an early stage (1.5-3 mo)
followed by B cell infiltration (6 mo). When the fraction enriched with
parietal cells, which were intensively stained with sera of AIG-bearing
mice and fluorescent antibody to mouse immunoglobulin G, was injected into
the foot pads of AIG-bearing nude mice, typical delayed-type hypersensitivity reaction was observed in all animals. This was not seen
in the mice injected with the cell fraction enriched with chief cells, although a few of them were stained by the immunofluorescent technique.
Thus, the delayed-type hypersensitivity reaction seems to be directly
involved in the mechanism of tissue damage.

L8 ANSWER 17 OF 23 MEDLINE DUPLICATE 6
AN 86006870 MEDLINE
DN 86006870
TI Effector mechanisms of syngeneic anti-tumour responses in mice. II.
Cytotoxic T lymphocytes mediate neutralization and rejection of radiation-induced leukaemia RL male 1 in the nude mouse system.
AU Keyaki A; Kuribayashi K; ***Sakaguchi S*** ; Masuda T; Yamashita J;
Handa H; Nakayama E
SO IMMUNOLOGY, (1985 Sep) 56 (1) 141-51.
Journal code: GH7. ISSN: 0019-2805.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198601
AB We demonstrated the efficacy of a long-term cultured cytotoxic T-lymphocyte line, CTLL-D4, on tumour growth inhibition using athymic nude
mice as recipients. CTLL-D4, specific for a unique surface determinant on
a radiation-induced leukaemia RL male 1 of ***BALB*** /c origin, was
obtained from the limiting dilution culture of MLTC cells performed
between spleen cells of a CB6F1-nu/+ mouse immunized in vivo and RL male 1
stimulator cells, and cultured for several months in the absence of added
TCGF as described in our preceding paper (Kuribayashi, 1985). The specific
inhibition of tumour growth by CTLL-D4 was demonstrated both in Winn-type
neutralization assay and in systemic transfer experiments. A subcutaneous
inoculation of the mixture of CTLL-D4 and RL male 1 cells resulted in the
complete inhibition of tumour growth, even at the effector to tumour cell
ratio of 1:1, whereas non-cytolytic D4f, which was self-Ia
antigen(s)-reactive, composed entirely of Lyt-1+23- T cells and derived
originally from CTLL-D4 but completely lost its cytotoxic activity during
culture with the irradiated syngeneic feeder cells alone, had no inhibitory effect at all. In the adoptive transfer studies, the
subcutaneously established tumours were rejected by the single i.v.
transfer of 2 X 10(7) CTLL-D4 cells into CB6F1-nu/nu mice. However, D4f
was ineffective again in this systemic transfer system. When the effect of
CTLL-D4 cells on tumour rejection in vivo was compared to that of non-cultured spleen cells hyperimmunized with RL male 1 cells, the former
exhibited more rapid rejection in nude mice after i.v. transfer than the
latter did, suggesting that CTLL-D4 cells also attack the tumour cells
much more effectively as effectors in vivo. Thus, it is conceivable that
CTLs are mainly involved in tumour rejection in this adoptive transfer
system using RL male 1 tumour cells and athymic nude mice.

L8 ANSWER 18 OF 23 MEDLINE DUPLICATE 7
AN 86006869 MEDLINE
DN 86006869
TI Effector mechanisms of syngeneic anti-tumour responses in mice. I.
Establishment and characterization of an exogenous IL-2-independent
cytotoxic T-lymphocyte line specific for radiation-induced leukaemia RL
male 1.
AU Kuribayashi K; Keyaki A; ***Sakaguchi S*** ; Masuda T
SO IMMUNOLOGY, (1985 Sep) 56 (1) 127-40.
Journal code: GH7. ISSN: 0019-2805.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198601
AB A CTL line (CTLL-D4) mediating specific cytolytic activity against
radiation-induced leukaemia RL male 1 has been established and maintained
on a long-term basis without the addition of exogeneous TCGF. This line
was originally selected by the limiting dilution of MLTC cells from RL
male 1-immune (***BALB*** /c X C57BL/6) F1-nu/+(CB6F1-nu/+) spleen
cells (500 cells/well) in the presence of 5% rat TCGF, 2000
rads-irradiated normal CB6F1-nu/+ spleen cells as the feeder cells, and
10,000 rads-irradiated RL male 1 tumour cells as the stimulator. After
expansion only with the feeder and tumour cells, CTLL-D4 shows highly
specific cytotoxic activity against RL male 1 by in vitro CMC assay, since
cells such as RL male 6, RL female 8, RL female 9, P815, MOPC-315 (H-2d),
EL-4 (H-2b) and YAC (H-2a) are not killed. Microcytoxicity assay of this
line has revealed that CTLL-D4 comprises three subsets of T lymphocytes
(100% Thy-1.2+): 15-25% Lyt-1+23-, 60-75% Lyt-1+23+ and 10-15% Lyt-1-23+.
The proliferation of this line seems to depend largely upon the syngeneic
MLR-like responsiveness of the Lyt-1+23- subsets of CTLL-D4 to the
Ia-positive cells in CB6F1-nu/+ splenic feeder cells, and has been restricted to the H-2d-haplotype of the feeder cells. In spite of the
vigorous cell proliferation by coculturing with the feeder cells alone,
the cytolytic activity of this line begins to decrease after some 7 days
of culture in the absence of the stimulator RL male 1 cells which have no
capacity to stimulate by themselves. Thus, by long-term culture of CTLL-D4
with the syngeneic feeder cells alone, a new non-cytolytic line (D4f) was
established. Mechanisms enabling the long-term maintenance of CTL activity
and subset composition have been discussed in terms of cellular cooperation between the subsets of this line.

L8 ANSWER 19 OF 23 MEDLINE
AN 85106930 MEDLINE
DN 85106930
TI Organ-specific autoimmune diseases induced in mice by elimination of T
cell subset. I. Evidence for the active participation of T cells in natural self-tolerance; deficit of a T cell subset as a possible cause of
autoimmune disease.

AU ***Sakaguchi S*** ; Fukuma K; Kuribayashi K; Masuda T
NC AG 04362 (NIA)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1985 Jan 1) 161 (1) 72-87.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198505
AB Organ-specific autoimmune diseases such as oophoritis, gastritis, thyroiditis, and orchitis were induced in female or male nude (nu/nu) mice by the transfer of nu/+spleen cells from which particular Lyt T cell subset(s) had been removed: nu/+spleen cells treated with anti-Lyt-1 plus complement (C) caused disease in recipient nude mice; anti-Lyt-2 plus C-treated spleen cells, in contrast, did not. The cells responsible for disease induction are believed to be Thy-1+, Lyt-1-, 2,3- (Thy-1, Lyt-1, 2,3), since spleen cells treated with mixed antisera, including anti-Lyt-1 and anti-Lyt-2, plus C, could induce the disease with almost the same incidence as anti-Lyt-1 plus C-treated cells (oophoritis 50%, gastritis 25%, thyroiditis 10-20%, and orchitis 40%). Cells treated with mixed antisera of anti-Thy-1, anti-Lyt-1, and anti-Lyt-2, plus C, could not induce autoimmune disease. Each induced autoimmune disease could be adoptively transferred to other nude mice via spleen cells, with resulting histological lesion of corresponding organs and development of specific circulating autoantibodies. Since anti-Thy-1 plus C treatment of donor spleen cells abrogated the capacity to transfer the disease, we conclude that T cells are required as effector cells, and that these may develop from Lyt-1-, 2,3- cells. Lyt-1+, 2,3- cells were demonstrated to have suppressive activity upon the development of the diseases; induction of autoimmunity was completely inhibited by the cotransfer of Lyt-1+, 2,3- cells with Lyt-1-, 2,3- cells. When anti-Lyt-2 plus C-treated cells (i.e., Lyt-1+, 2,3- and Lyt-1-, 2,3- cells) were mixed with anti-Lyt-1 and anti-Lyt-2 plus C-treated cells (i.e., Lyt-1-, 2,3- cells) in various ratios, then transferred to nude mice, the development of each autoimmune disease was clearly inhibited, even by small doses of Lyt-1+, 2,3- cells. The autoimmune disease we were able to induce was quite similar to human organ-specific autoimmune disease in terms of the spectrum of organs involved, histopathological features, and the development of autoantibodies to corresponding organ components (oocytes, parietal cells, thyroid colloid, including thyroglobulin, and sperm).(ABSTRACT TRUNCATED AT 400 WORDS)

L8 ANSWER 20 OF 23 MEDLINE
AN 82191010 MEDLINE
DN 82191010
TI A cloned cell line, Mk1, possessing Ia antigens and accessory cell activity.
AU Kyoizumi S; Noro N; Teshigawara K; ***Sakaguchi S*** ; Masuda T
NC NOI-CP7-1003 (NCI)
SO JOURNAL OF IMMUNOLOGY, (1982 Jun) 128 (6) 2586-94.
Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198209

L8 ANSWER 21 OF 23 MEDLINE DUPLICATE 8
AN 83084567 MEDLINE
DN 83084567
TI Study on cellular events in postthymectomy autoimmune oophoritis in mice. I. Requirement of Lyt-1 effector cells for oocytes damage after adoptive transfer.
AU ***Sakaguchi S*** ; Takahashi T; Nishizuka Y
NC NO1 CP55650 (NCI)
NO1 CP71003 (NCI)
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1982 Dec 1) 156 (6) 1565-76.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198304
AB Neonatal thymectomy during the critical period, 2-4 d after birth, can induce various organ-specific autoimmune diseases including oophoritis in A/J mice. The oophoritis thus induced was passively transferred into neonatal mice by injection of spleen cells obtained from syngeneic donors with the disease. Recipient ovaries were rapidly damaged with remarkable mononuclear cell infiltration and destruction of follicular structures. The phenotype of effector cells responsible for successful adoptive transfer was found to be Thy-1+, Lyt-1+,23-, Ia-, Qa-1-, and was sensitive to antithymocyte serum treatment but resistant to cyclophosphamide treatment or in vitro X-ray irradiation. The compatibility between donor and recipient at the major histocompatibility complex was not required for the effector phase of transfer. The oophoritis induced in ***BALB*** /c (nu/+ or +/+) was also shown to be transferred into athymic ***BALB*** /c nude mice with resulting ovarian lesion and circulating autoantibodies against oocytes. In this transfer system, the effector cells were also demonstrated to be T cells with the Lyt-1+,23- phenotype. Adoptive transfer experiments in both systems revealed that the destruction of ovaries in postthymectomy autoimmune oophoritis was mediated by Lyt-1 T cells. Whether these T cells can be distinguished from other Lyt-1 cells, such as T helper cells and effector T cells in delayed-type hypersensitivity (DTH), is not clear at present, but the results suggest that the effector mechanisms may be closely related to a DTH reaction.

L8 ANSWER 22 OF 23 MEDLINE
AN 82123423 MEDLINE
DN 82123423
TI Bacteriological and epidemiological approaches to the prophylaxis of enteric infection. VI. In vitro studies on the mechanism of acquired resistance to Shigella flexneri infection (1).
AU Sakaguchi T; ***Sakaguchi S*** ; Okamoto M; Matsui S; Anzai H
SO KITASATO ARCHIVES OF EXPERIMENTAL MEDICINE, (1980 Dec) 53 (3-4) 97-109.
Journal code: KVS. ISSN: 0023-1924.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 198206

L8 ANSWER 23 OF 23 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82119347 EMBASE
DN 1982119347
TI Bacteriological and epidemiological approaches to the prophylaxis of enteric infection. VI. In vitro studies on the mechanism of acquired resistance to Shigella flexneri infection.
AU Sakaguchi T.; ***Sakaguchi S.*** ; Okamoto M.; et al.
CS Japan

SO Kitazato Archives of Experimental Medicine, (1980) 53/3-4 (17-29).
CODEN: KAEMAW
CY Japan
DT Journal
FS 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
048 Gastroenterology
LA English
AB Experiments on defence mechanism against Shigella infection were carried out in vitro using Sh. flexneri 2b, 17-A (virulent strain), Sh. flexneri 2b, 17-N (avirulent strain), the euthenic ICR male mice, and the congenitally athymic ***BALB*** /cA (nu/nu) male mice. Adherent cells (macrophages) from peritoneal cavity of normal mice were still-stained-cultured, and the virulent strain was allowed to infect these adherent cells, and then peritoneal non-adherent cells (lymphocytes) from immunized mice were added to them at proper times. Experiments were conducted on rate of infection for the macrophages and grades of intracellular bacterial growth. The findings of the experiments may be summarized as follows: Macrophages taken from euthenic mice as well as athymic mice immunized with the virulent strain were more effective than normal macrophages in reducing the rate of Shigella infection and inhibiting bacterial growth. Normal macrophages suppressed the infection of the virulent strain, only when they were infected in the presence of lymphocytes from mice immunized with the virulent strain. However, even when these immunized lymphocytes were added in advance to normal macrophages and then were washed away before the virulent strain started to infect, the infection and intracellular bacterial growth were not inhibited. Experiments on the infection of the virulent strain to normal macrophages were also carried out in the presence of normal lymphocytes or immunized lymphocytes against avirulent strain. However, decrease in infection rates and inhibition of intracellular bacterial growth were not observed. Lymphocytes from nude mice immunized with the virulent strain, like lymphocytes from normal mice, were observed to have no tendency to inhibit Shigella to infect normal macrophages or suppress intracellular bacterial growth. From these experiments, it was shown that the acquired active immunity against Shigella infection might involve the action of thymus-independent immune macrophages as well as the action of normal macrophages activated by the co-existence of thymus dependent immune lymphocytes and Shigella bacillus.

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L4 6 S L3 AND BALB?/AB,BI
L5 4 DUP REM L4 (2 DUPLICATES REMOVED)
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